Breakthrough Innovations for better and healthier Crops

“KeyGene’s views for the future”

Arjen J van Tunen, CEO KeyGene

Crop Innovation & Business 2019
KeyGene
the Crop Innovation Company

1989; Visionary group of breeders, embracing the opportunity of biotech

1989 – 2019; From Technology & Trait Provider to Crop Innovation Company

“Our Innovation Platforms work in harmony to provide integrated solutions for current and future crop challenges”
Our World of Today

Our ever changing world: what is happening?

Major developments:

- China, India economies: economic growth slows down; growth in 2019 in Europe 1.3%; NL with 1.9% still fine
- Impact of trade wars
- Enormous consolidations in the industry to big 4 that now all combine seeds, agro chemicals and GM: 1. Bayer (with Monsanto), 2. Corteva (Ag Dow & Ag Dupont), 3. Syngenta / Chinachem, 4. BASF
- New competition: nice varieties developed by many requires transformational new varieties from the leading seed companies which make a difference in the market
- Major VC investments in Agri domain (e.g. USA)
  Need now to monetize investments
Our World of Today

Our ever changing world: what is happening?

Major developments:

- Need for more, healthy and better food e.g. via fruits and vegetables
- Need for sustainable agricultural production
- Need to adapt to climate change
- Need for data management, AI and Machine learning at all levels through the food demand chain. New entrants like MicroSoft, Amazon Web Services and IBM
- Need for more and new forms of alliances and collaborations

Requires the development of:
Breakthrough Technologies, Better Traits & New and Improved Crops
Breakthrough Technologies
Genomics & Phenomics

• **Mainstream Farming**: using varieties developed via crossing and selection supported by DNA technologies and Genomics
  
  *Large track record of good quality products developed sold for acceptable price*

• **Large-scale Farming**: using varieties developed via GM, Gene Editing & Big Data:
  - corn, soybean, canola, cotton, sugar beet at multinationals
  
  *Large scale, cost effective for farmer, data-driven, innovative, risk perception often high (esp. in EU, Japan and for Food also in China and India)*

• **Organic Farming**: using varieties developed via traditional crossing and selection, no GM, Genomics and MAB ok, no chemicals, low yields
  
  *Currently niche activities but growing*

• **New: Vertical Farming**: production in multiple layers in factories in our cities or at home. Leafy vegetables & herbs first. New adapted varieties wanted
  
  *I strongly embrace this because of food safety & sustainability & local production aspects. But: maybe too technical?*
Better Traits
Interesting “old” and new traits

• Yield & Yield Stability (feed the world, revolution in photosynthesis)
• Abiotic Stress Tolerance (adapt our crops to climate change)
• Biotic Stress Resistances (sustainability, reduce the use of agro chemicals)
• Quality, Taste (to serve more middle class consumers)
• Long shelf life (stop reducing waste!)
• Health (longer, better life for all of us)

Besides some new traits, many “old” traits are still of high interest
New and Improved Crops

Genomics and Phenomics enables innovations in all crops

- **Accelerate** improvement of current cash crops (e.g. corn, soybean, tomato, lettuce)
- **Increase** improvement of small crops (e.g. ornamentals, berries)
- **Start** improvement of plantation crops (e.g. oil palm, banana)
- **Start** improvement of difficult and polyploidy crops (e.g. onion, potato, wheat, strawberry)
- **Enable** improvement of orphan & vegetatively propagated crops (e.g. cassava, millet, plantain, trees)
- **Domesticate** and develop new crops (e.g. dandelion for rubber, stevia for sweetener)

*Because of cost reductions and high throughput & specificity in genomics and phenomics we can now molecularly improve crops that we could not touch before*
DNA: source of genetic information
DNA the basis for breeding: since 1953

DNA has 4 building blocks (GATC)
Not digital but quatro-code
In all plant cells
DNA: source of genetic information
DNA from each crop plant differs = genetic variation!

Tomato DNA consists of 1.000.000.000 code letters (human: 3 x more)
In DNA of 2 different commercial tomato plants: ~ 500.000 differences
With a third plant: ~ 800.000 differences
In 100 different commercial tomato varieties: ~ 10 million differences
Between commercial and wild tomato species: ~ 100 million differences

Molecular Plant Breeding

Which DNA differences are important?
How can we increase the amount of useful differences?
Which differences can we use to develop better crops in a non GM way?
Breakthrough Technologies

Paradigm shifts in sequencing: Cost ↓ Quality ↑

HT Short Read Sequencing

PromethION
HT + Long Read Sequencing

Long Read Sequencing
Plant genomes can be **large**
- From 100 Mbp to 150 Gbps

Plant genomes can be **complex**
- Repeats
- Heterozygosity
- Polyploidy
- Large variation

**Cotton**
- 4n $\approx$ 2.3 Gb
- ~89% repetitive sequences

**Common Wheat**
- 6n $\approx$ 17 Gb
- ~80% repetitive sequences

**Pepper**
- 2n $\approx$ 3.5 Gb
- ~81% repetitive sequences
- Qin et al. (2014) PNAS 111: 5135 – 5140

**Melon**
- 2n $\approx$ 0.4 Gb
- low-copy DNA

**Tomato**
- 2n $\approx$ 0.9 Gb
- low-copy DNA

**Onion**
- 2n 16 Gb
- Currently sequencing
Trait Discovery - KeySeeQ®
Transcriptomics based discovery

Objective & biological Questions
Experimental design:

Biological experiment

Data analysis 1
Data to sequences per sample & per gene

30,000 genes

Data analysis 2
Differences per sample per gene

5,000 genes

Selection
Biologically relevant signals, genes & pathways

500 genes

Biological experiment validation

50 genes

Biological Expert Knowledge

Candidate Genes

The crop innovation company
CropPedia
Powerful data analysis & visualization platform

- How to handle these big data?
- Think Google for Plant genetics & genomics
- In-house software for improved decision making

Interactive easy to use
Proprietary & public data
Any crop
Adopted by many

“This is a response to our need for one platform which integrates and visualizes all data and knowledge”

Bio-informatician Top 5 Global breeding company
Breakthrough Technologies

KeyPoint® Breeding

**Mutagenesis**

+ Chemical Mutagen (eg EMS)

**Grow Mutagenized Population**

**Isolate DNA Pool DNA**

Screen for mutation In your genes of interest

**Selection & verification of novel variant plants**

**Targeted detection novel variants**

**GENOTYPE & PHENOTYPE**

Pre-breeding material with mutation in your Gene of interest
KeyPoint® Breeding
KeyGene’s Sequence Based, non GM Mutation Detection System

For many Crops:

Vegetables
Tomato, Sweet & Hot Pepper, Cabbage, Cucumber, Melon

Field Crops
Potato, Rye, Wheat, Sugar Beet, Tobacco, Dandelion, Soybean, Corn, Canola, Sorghum, Rice, Barley, Cassava, Sunflower

Flowers
Ornamental Sunflower

In-house industrialized procedure in one run:

- 4,000 – 25,000 mutagenized plants
- up to 20 genes simultaneously screened
- non-GM with patentable mutations
- combined with KeySeeQ® gene discovery system
- linked to strong allele selection prediction
- many mutants phenotyped in KeyGene’s robotized and automated phenotyping system: PhenoFab®
Breakthrough Technologies

PhenoFab® Phenotyping

Applications:

• phenotype hundreds of KeyPoint mutants
• characterize biologicals
• characterize growth substances
• assay root nematode resistances
• ... and many others
PhenoFab® Data management

Data Management:
• 400 plants x 9 pictures / plant x 35 days = 126,000 digital images!

Deploy:
• Interactive data mining in PhenoReport
• VR Breeding Tool
Breakthrough Technologies result in the development of Better Traits in New and Improved Crops in close collaboration with partners all over the world
Better Traits
Sucking Insect Resistance in tomato

Sucking Insects are a big problem especially in the Tropics.

Algorithms developed for phenotyping of insects on plants:
Larvae – Eggs - Adults
Downey Mildew did hit the Impatiens market hard in 2011. After genome sequencing combined with genotyping and phenotyping resulted in a fast and effective introgression of a resistance source.

Ball Horticultural’s position as market leader was reconfirmed with introduction of Beacon impatiens.
Better Traits

Improved rice - Trials Italy, Po Delta 2016

KeyPoint® Breeding resulted in rice with a single base pair mutation that has higher yield and erect panicles.

Rice is a main staple food all around the world including Europe where we have “Risotto” rice production in the Po delta.
KeyPoint® Breeding resulted in virus resistant pepper and other crops with single base pair mutation.

To be further announced at the MPMI conference in Glasgow, 14th July 2019 by Prof Marcel Prins, KeyGene
New and Improved Crops

Genomics & Phenomics enables development of new and improved crops

Improved Crops:

• Numerous vegetables, field crop and plantation crops

New Crops:

• Stevia for natural sweeteners
• Medicinal cannabis for cannabinoids
• Lupines for plant proteins
• Banana for bananas
• Dandelion for natural rubber

Banana flowering in Wageningen, Netherlands

Lupinus albus
New and Improved Crops

Breakthrough: sustainably produced natural rubber

Natural rubber remains essential in today’s economy. The production is however exposed to threats, including price/supply volatility, diseases and environmental concern linked to SE Asia deforestation.

KeyGene used own genomics to develop the world first interspecies hybrid Dandelion variety “Flexilis® hybrid”. This novel agricultural crop enables annual rubber production in temperate climates.

Inuline as side product
Breakthrough Technologies result in the development of Better Traits in New and Improved Crops and vice-versa. New and Improved Crops and Better Traits require the development of Breakthrough Technologies.

… and this cycle goes on and on and on.

“Together with my KeyGene colleagues and all our partners, I am proud and thankful to be part of this Innovation Cycle that helps our societies forward and will enable us to feed the world.”

Arjen van Tunen, CEO KeyGene